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Therapeutic effects of pomegranate (*Punica granatum* L.) pith and carpellary membrane extract on lead-induced toxicity in rats

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Abstract

Pomegranate is an ancient edible fruit with various pharmaceutical bioactivities such as antioxidant, lipid regulation and anti-inflammation. In this study the effectiveness of pomegranate pith and carpellary membrane (PPCM) extract in treatment of experimental lead intoxication was assessed in rats. Female Wistar rats were exposed to 1000ppm lead acetate in drinking water for 35 days and treated thereafter with PPCM extiract (100 and 200mg/kg, orally) twice a day for 35 days. The concentration of lead in blood, kidney, liver, bone and brain were measured using atomic absorption spectrophotometry. Treatment with PPCM extract reduced lead retention in blood and tissues. With the highest dose of PPCM extract, the greatest rate of reduction of lead concentrations were observed in brain (61%), blood (53%), and bone (34.5%). No significant changes were observed in copper, zinc and iron concentration of serum and liver, in neither doses of PPCM extract. In conclusion it was demonestrated that PPCM and carpellary membrane had therapeutic effect in the treatment of lead intoxication without any side effects on essential elements in blood and tissues of rats.

Keywords: punica granatum, lead intoxication, microelements, rat

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Introduction

Lead is a soft, malleable non-essential heavy metal with neither beneficial nor desirable nutritional effects on animals and humans. It is widely used in various industrial products, such as storage batteries, automobile radiator, paint pigments, glass, weights, ceramic, plastic and mortar. Organo-lead compounds, such as tetraethyl and tetramethyl lead are also used as additives in certain gasolines particularly in developing countries (Kosnett 2001). On the other hand, lead is an industrial and environmental cumulative pollutant that affects all major organs inducing a broad range of physiological, biochemical and behavioral dysfunctions in both animals and humans (Patrick 2006a). Over the past few decades, along with lowering lead exposure, there has been growing evidence and concern that prolonged exposure to low levels of lead has proven serious risk factor for neurological, cardiovascular and reproductive diseases (Ahmed and Siddiqui 2007; Needleman 2009). Exposure to low levels of lead has been associated with behavioral abnormalities, learning impairment, decreased hearing, impaired cognitive functions and hypertension in human and experimental animals (Patrick 2006a; Patrick 2006b; Jakubowski 2011). Oxidative stress has been suggested as the primary mechanism for the pathogenesis of lead intoxication. Highly reactive oxygen species (ROS) produced aftermath of lead exposure may result in systemic mobilization and depletion of the cell intrinsic antioxidant defenses. Formation of ROS beyond the scavenging capacity of these antioxidant defense mechanisms results in accumulation of harmful free radicals and likelihood of oxidative damage of critical bio-molecules, such as enzymes, DNA, proteins and membranes lipids (Ahmed and Siddiqui 2007). The current approved treatment for lead intoxication is relied primarily on the administration of chelating agents that forms an insoluble complex with lead and removes the same from lead burdened tissue. However, most of these chelating agents suffer from many disadvantages (Domingo 1998; Kalia and Flora 2005). Administration of antioxidants such as vitamins and herbal drugs during chelation therapy has been found to be beneficial in increasing lead mobilization and providing recoveries in altered biochemical variables (Gurer and Ercal 2000; Hsu and Guo 2002; Patrick 2006b; Antonio-Garcia and Masso-Gonzalez 2008).

Pomegranate (*Punica granatum* L.), belongs to the family Punicacea and is an ancient edible fruit widely grown in Iran and some tropical and subtropical countries. It is known as a sacred fruit conferring powers of fertility, abundance, and good luck. It also features prominently in the ceremonies, art and mythology (Jurenka 2008). Pomegranate has been used in various regions and folk or traditional medical systems as a food supplement or a medicine because of its enormous compounds with lots of activities and without toxicity (Wang, Ding *et al*. 2010). Various pharmaceutical bioactivities such as antioxidant, lipid regulation, anti-hypertension, gastroprotection, hepatoprotection, anti-diarrhea, anti-helminthes, antibacterial, antivirus, anti-inflammation, anti-angiogenesis, anti-diabetes and immunomodulation, for pomegranate have been appointed (Li, Zhang *et al*. 2003; Huang, Peng *et al*. 2005; Haidari, Ali *et al*. 2009; Osman, Ahmed *et al*. 2011; Bhandari 2012; Jasuja, Saxena *et al*. 2012; Shiban, Al-Otaibi *et al*. 2012). El-Ashtoukhy (2008) used pomegranate pith, to remove lead from aqueous solution (El-Ashtoukhy, Amin *et al*. 2008). In the current investigation we studied the protective effect of PPCM and carpellary membrane extract against lead intoxication in rats.

Materials and methods

Pomegranate Pith and Carpellary

Membrane Extract preparation

Fresh pomegranates (Feizabad cultivar) were obtained from local market. PPCM and carpellary membrane were manually separated, dried in room temperature and powdered in a grinder. The powder was extracted using distilled water. The extract was filtered through a mesh for removal of particles. Fine particles were also separated by centrifugation at 4000g for 15min at 4˚C.

Animals and experimental design

Thirty two female Wistar rats weighing 170-200g were obtained from Razi Institute of Mashhad (Mashhad, Iran). The animals were kept in polypropylene cages and fed a standard pelleted laboratory animal diet (Javaneh Khorasan-Iran). The rats were allowed free access to food and water. The animals were allowed to acclimatize for 14 days before the experiment. Then, the rats were randomly divided into 4 groups (n=8). Group 1 was received no lead acetate in drinking water during the experiment. Group 2-4 was received 1000ppm lead acetate (Merck, Darmstadt, Germany) in drinking water for 35 days (Aslani, Najarnezhad *et al*. 2009). Group 2 was received no PPCM extract. Groups 3 and 4 were received 100 and 200 mg of PPCM extract, respectively, twice daily by stomach gavage for 35 days. At the end of the experiment the rats were anesthetized with ether, bled by cardiac puncture. Liver, kidney, brain and femur were removed. Liver was also used for measurement of essential elements, copper, zinc and iron. All the procedures concerning the use of animals were approved by the Animal Welfare Committee of Ferdowsi University of Mashhad.

Determination of lead in blood

Blood samples were dissolved in 65% nitric acid (Merck, Darmstadt, Germany) and ammonium vanadate (Merck, Darmstadt, Germany) and then centrifuged (2,500 rpm for 5 min) (Najar-Nezhad, Aslani *et al*. 2008). Lead concentrations were determined by atomic absorption spectrophotometer (Perkin-Elmer AS800, Massachusetts, U.S.A.) at 283.3 nm wave-lengths using graphite furnace.

Determination of lead, copper, zinc and iron in tissues

Tissue samples were digested in a 1:1 mixture of 95-97% sulfuric acid (Merck, Darmstadt, Germany) and 65% nitric acid (Merck, Darmstadt, Germany), with a slight modification of the wet-ashing technique (Najar-Nezhad, Aslani *et al*. 2008). Lead, copper, zinc and iron concentrations were determined by atomic absorption spectrophotometer (Perkin-Elmer AS800, Massachusetts, U.S.A.) at 283.3, 324.8, 248.3 and 213.9 nm wave-lengths, respectively. Lead was measured through graphite furnace atomic absorption spectrometry (Table 1) and Flame atomic absorption spectrometry was used for measurement of liver copper, zinc and iron (Table 2). The certified reference material NIST-1577C (bovine liver) was used for validation purposes. Detection limits were defined as 3 times the standard deviation of an average of procedural blanks. The corresponding values for lead, copper, zinc and iron were obtained equal to 0.03, 0.1 0.3 and 0.1ppb. The repeatability of the measurement of the analytical signals usually was not worse than 1% (Table 3). To control the stability of the analytical signals the measurements for the standard solutions were repeated before and after measurements of the samples.

Table 1. Instrumental conditions for determination of lead in liver.

Metal	Wavelength (nm)	Slit width (nm)	temperature (°C) Drying,	Ashing	Atomization	Cleaning	Injection volume (µl)
Pb	283.3	0.7	120-400	850	1800	2450	20

Table 2. Instrumental conditions for determination of copper, zinc and iron in liver.

Metal	Wavelength, nm	Slit width, nm	Flame type
Cu	324.6	0.7	Air–acetylene, oxidizing
Zn	248.3	0.2	Air–acetylene, oxidizing
Fe	213.9	0.7	Air–acetylene, oxidizing

Table 3. Comparison of the found and certified values of lead, copper, zinc and iron in the certified reference material.

Certified material		Bovine liver NIST-1577C
Pb	Certified value ppb	62.8
	Found ppb	62.77
	Recovery (%)	99.95
Cu	Certified value ppm	275.2
	Found ppm	275.2
	Recovery (%)	100
Zn	Certified value ppm	181.1
	Found ppm	181.1
	Recovery (%)	100
Fe	Certified value ppm	197.94
	Found ppm	197.94
	Recovery (%)	100

Determination of copper, zinc and iron in serum

Serum concentration of copper, zinc and iron were determined by an automated chemistry analyzer (Biotecnica Targa 3000, Rome, Italy) using commercial kits (Shimazmoon, Tehran, Iran for copper; Giesse Diagnostic, Rome, Italy for zinc; and Parsazmoon, Tehran, Iran for iron). The data were checked for errors and compared with written reports. Out layers were rechecked to ensure that values were accurate.

Statistical analysis

The statistical analyses were carried out using the SPSS 11.5 software (SPSS Inc., Chicago, IL, U.S.A.). The significance of difference was evaluated by one-way analysis of variance (ANOVA) followed by Bonferroni procedure to compare means among different groups. Results are expressed as mean ± standard deviation and significance was defined as values of $p<0.05$.

Results

Lead concentration in blood and tissues

Lead concentration in various tissues of rats exposed to lead is given in Table 4. For lead exposed untreated group (group II), the distribution of lead was in the following order: bone > kidney > liver > blood > brain. Lead treated animals showed significantly ($p < 0.05$) higher levels of lead in blood, liver, kidney, bone and brain compared to those of the control animals. Groups treated with PPCM and carpellary membrane extract (groups III and IV) had entire body tissues lead burden (2.57 and 2.41µg/kg respectively) significantly ($p < 0.05$) lower than that of lead exposed untreated group (3.30µg/kg).

Table 4. Lead concentration in blood (µg/l) and tissues (µg/gr) of various groups

Group	Blood	Liver	Kidney	Brain	Bone
I	0.043±0.030^{a}	0.192±0.031^{a}	0.257±0.025^{a}	0.002±0.000^{ad}	1.932±0.198^{a}
II	64.434±10.792^{bc}	0.309±0.128^{a}	2.474±0.197^{b}	0.044±0.004^{b}	10.527±0.609^{b}
III	50.507±5.961^{cd}	0.160±0.040^{a}	1.390±0.230^{cd}	0.025±0.008^{bc}	8.729±0.778^{bc}
IV	30.445±19.152^{abd}	0.373±0.127^{a}	2.215±0.424^{bd}	0.017±0.006^{cd}	6.898±1.575^{cd}

Mean ± S.D. (eight values). In each column, a, b, c and d was significantly differed ($p<0.05$)

Moreover, kidney lead concentration of group treated with 100mg/kg PPCM and carpellary membrane extract (group III) was significantly ($p < 0.05$) lower than that of lead exposed untreated group (group II); and blood, brain and bone lead concentration of group treated with 200 mg/kg PPCM and carpellary membrane extract (group IV) was significantly ($p < 0.05$) lower than those of lead exposed untreated group (group II).

Liver and serum concentration of copper, zinc and iron

Copper, zinc and iron concentration in liver and serum of various groups are given in Table 5 and Table 6, respectively. Groups treated with PPCM and carpellary membrane extract (groups III and IV) had liver copper, zinc and iron burden lower than those of lead exposed untreated group (group II), but this reduction was not significant ($p>0.05$). Group treated with 100mg/kg pomegranate pith and carpellary membrane extract (group III) had serum copper, zinc and iron burden lower than those of lead exposed untreated group (group II), but this reduction was not significant ($p>0.05$). Group treated with 200 mg/kg capillary and carpellary membrane extract (group IV) had lower serum copper and more serum zinc and iron burden than those of lead exposed untreated group (group II), but these changes were not significant (carpellary >0.05).

Table 5. Copper, zinc and iron concentration in liver (µg/gr) of various groups

Group	Cu	Zn	Fe
I	4.880±0.596	25.750±0.590	341.18±36.915
II	4.185±0.291	25.250±0.750	324.35±20.113
III	3.228±0.481	23.925±2.303	283.25±30.539
IV	3.093±0.852	21.433±3.404	309.70±62.328

Mean ± S.D. (eight values).

Discussion

Many compounds have been experimented in animal models for treatment of lead intoxication (Khan, Mostofa *et al*. 2008; Aslani, Najarnezhad *et al*. 2009; Alcaraz-Contreras, Garza-Oca˜nas *et al*. 2011; Aslani, Najarnezhad *et al*. 2011). Pomegranate (*Punica granatum* L.) is an ancient edible fruit with various pharmaceutical bioactivities (Wang, Ding *et al*. 2010). In this study the administration of different doses of PPCM and carpellary membrane extract to lead exposed rats significantly lowered tissue lead levels. The present study is the first report that showed pomegranate could reduce lead in the body. PPCM and carpellary membrane extract at a dose of 200 mg/kg was more effective in removing lead from bone and brain. Several studies have revealed that at least some portion of lead in the bone is accessible to chelators, as evidenced by the fact that EDTA and DMSA can reduce lead concentrations in the bone (Cory-Slechta, Weiss *et al*. 1987; Tendon, Singh *et al*. 1994; Jones, Singh *et al*. 1997), however, PPCM and carpellary membrane extract has several advantages over those chelators. First of all PPCM extract is a natural product and there is no report for its side effect, while several adverse effects have been reported for conventional lead chelators (Gwaltney-Beant 2003; Meldrum and Kok 2003; Casteel 2006). Furthermore, PPCM and carpellary membrane extract has antioxidant activity (Shiban, Al-Otaibi *et al*. 2012) and may depress pathogenesis of lead intoxication. There are convincing data showing that lead toxicity is associated with oxidative stress and an increase in production of reactive oxygen species (Patrick 2006b; Anderson and Adenuga 2007). It has been shown that

phenolic compounds have antioxidant activity and can reduce blood lead levels (Aksu, Didin *et al*. 2012). Pomegranate is a fruit rich of various polyphenolic compounds such as tannins, flavonoids, alkaloids, organic acids (Wang, Ding *et al*. 2010), so it can decrease the blood and tissues lead levels by reducing the absorption of lead from gastrointestinal tract and/or by limiting the retention of lead in metabolism.

Table 6. Copper, zinc and iron concentration in serum (µg/dl) of various groups

Group	Cu	Zn	Fe
I	299.88±10.246	134.12±8.711	319.62±19.998
II	330.50±11.712	199.00±18.139	328.00±15.552
III	269.14±13.702	133.71±9.551	298.29±13.525
IV	263.76±39.388	228.80±99.344	392.80±44.903

Mean ± S.D. (eight values).

Some degrees of mineral depletion, copper and zinc in particulars, are an adverse effect associated with administration of most of current heavy metal chelators (Anderson 1999; Kalia and Flora 2005). Although the clinical importance of such effects is not fully understood, it is suggested that teratogenic potential of most chelators is, at least in part, due to induced trace element deficiencies (Taubeneck, Domingo *et al*. 1992; Domingo 1998). In the present study no adverse effect on copper, zinc or iron concentration of serum and liver was seen following PPCM and carpellary membrane extract administration.

Different doses of lead have been used to induce lead intoxication in rats and to study therapeutic efficacy of different compounds (Patra and Swarup 2004; Alabbassi, Hussain *et al*. 2008; Arrak 2010; Kilikdar, Mukherjee *et al*. 2011). A dose of 1000 ppm lead through drinking water for 35 days has significantly increased blood and tissues lead values. The highest accumulation of lead was detected in bone, followed by kidney, liver, blood and brain. This could be due to different bio-kinetic pattern of lead distribution in various tissues (Thuppil and Kaushik 2012). The bone is recognized as a tissue to store a considerable portion of the body burden of lead (Zmudzki, Bratton *et al*. 1983) so the highest lead concentration in the bone observed in this study was not unexpected. The lowest concentration of lead was observed in the brain. The brain has low lead uptake capacity, but it has high tenacious lead retention capacity. Moreover, lead is distributed unevenly in the brain, which depends on the amount of lead exposure. At low levels, the lead concentration in different regions of the brain is significantly correlated with the potassium concentrations, indicating that lead is mostly accumulated in the cell rich parts of the brain like the hippocampus (Grandjean 1978; Petit, Alfano *et al*. 1983). Only at very high concentrations of lead, the blood-brain barrier is broken and lead enters neuronal tissue (Thuppil and Kaushik 2012).

Alonso *et al*. (2004) stated metal binding regions of metallothionines, which is increased in lead intoxication, have also specific area for copper and zinc, so lead can disrupt trace element metabolism (Klaassen, Liu *et al*. 1999; Alonso, Montana *et al*. 2004). In this study copper, zinc and iron levels in serum and liver of lead exposed rats (group 2) did not differ compared to those of negative control rats (group 1).

The present study is the first report that showed pomegranate could reduce lead in the body without any significant ($p<0.05$) depletion of copper, zinc or iron concentration of serum and liver.

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References

Ahmed, M. and Siddiqui, M. (2007). Low level lead exposure and oxidative stress: current opinions. *Clinica Chemica Acta*, **383**, 57-64.

Aksu, D.S., Didin, M. and Kayikci, F. (2012). The protective role of polyphenols on blood cells in rats exposed to lead. *Revista Român ăde Medicinăde Laborator*, **20**, 233-243.

Alabbassi, M.G. and Hussain, S.A. (2008). Therapeutic Effects of Melatonin in Lead-Induced Toxicity in Rats. *Iranian Journal of pharmaceutical Research*, **17**, 47-54.

Alcaraz-Contreras, Y.L., Garza-Oca˜nas, L., Carca, K. and Ram, S. (2011). Effect of Glycine on LeadMobilization, Lead-Induced Oxidative Stress, and Hepatic Toxicity in Rats. *Journal of Toxicology*, *doi: 10.1155/2011/43.539*

Alonso, M.L., Montana, F.P., Miranda, M., Castillo, C., Hernandez, J. and Benedito, J.L. (2004). Interactions between toxic (As, Cd, Hg and Pb) and nutritional essential (Ca, Co, Cr, Cu, Fe, Mn, Mo, Ni, Se, Zn) elements in the tissues of cattle from NW Spain. *BioMetals*, **17**, 389-397.

Anderson, B.O. and Adenuga, G.A. (2007). Effect of lead exposure on liver lipid peroxidative and antioxidant defense systems of protein-undernourished rats. *Biological Trace Element Research*, **116**, 219–225.

Anderson, O. (1999). Principles and recent developments in chelation treatment of metal intoxication. *Chemical Reviews,* **99**, 2683–2710.

Antonio-Garcia, M. and Masso-Gonzalez, E. (2008). Toxic effects of perinatal lead exposure on the brain of rats: Involvement of oxidative stress and the beneficial role of antioxidants. *Food and Chemical Toxicology*, **46**, 2089-2095.

Arrak, J.K., (2010). Effect of Ellagic Acid Extracted from Pomegranate (Punica granatum L.) on Thyroid and Parathyroid Gland of Adult Rats Exposed to Lead Acetate. *Kufa Journal For Veterinary Medical Sciences*, **1**, 39-51.

Aslani, M., Najarnezhad, V. and Mohri, M. (2009). Individual and Combined Effect of Meso-2,3-Dimercaptosuccinic Acid and Allicin on Blood and Tissue Lead Content in Mice. *Planta Medica*, **76**, 241-244.

Aslani, M.R., Najarnezhad, V. Mohri, M., and Azad, M. (2011). The effect of allicin on blood and tissue lead content in mice. *Comparative Clinical Pathology*, **20**, 121-125.

Bhandari, P.R. (2012). Pomegranate (Punica granatum L). Ancient seeds for modern cure? Review of potential therapeutic applications. *Internatial Journal of nutrition Pharmacology Neurological Diseases*, **2**, 171-184.

Casteel, S.W. (2006). Lead. Small Animal Toxicology. M. E. Peterson and P. A. Talcott. Louis, Saunders, 795–805.

Cory-Slechta, D.A., Weiss, B. and Cox, C. 1987. Mobilization and redistribution of lead over the course of calcium distribution of lead over the course of calcium disodium ethylenediaminetetra acetate chelation therapy. *Journal of Pharmacology and Experimental Therapeuties*, **243**, 804–813.

Domingo, J. (1998). Developmental toxicity of metal chelating agent. *Reproductive Toxicology*, **12**, 499-510.

El-Ashtoukhy, E.Z., Amin, N.K. and Abdelwahab, O. (2008). Removal of lead (II) and copper (II) from aqueous solution using pomegranate peel as a new adsorbent. *Desalination*, **223**, 162-173.

Grandjean, P. (1978). Regional distribution of lead in human brains. *Toxicology Letters*, **2**, 65-69

Gurer, H. and Ercal, N. (2000). Can antioxidants be beneficial in the treatment of lead poisoning? Free *Radical Biology and Medicine*, **29**, 927-945.

Gwaltney-Beant, S. (2003). Lead. Clinical Veterinary Toxicology. K. H. Plumlee. Louis, Mosby, S.t. 204–210.

Haidari, M., Ali, M. and Cabrini, R.L. (2009). Pomegranate (Punica granatum) purified polyphenol extract inhibits influenza virus and has a synergistic effect with oseltamivir. *Phytomedicine*, **16**, 1127-1136.

Hsu, P. and Guo, Y. (2002). Antioxidant nutrient and lead toxicity. *Toxicology*, **180**, 33-44.

Huang, T.H., Peng, G., Prasad Kota, B., Qian Li, G., Yamahara, J., Roufogalis, B.D. and Li, Y. (2005). Pomegranate flower improves cardiac lipid metabolism in a diabetic rat model: role of lowering circulating lipids. *British Journal of Pharmacology*, **145**, 767–774.

Jakubowski, M. (2011). Low-level environmental lead exposure and intellectual impairment in children- the current concepts of risk assessment. *International Journal of occupational Medicine and Environmental Health*, **24**, 1-7.

Jasuja, N.D. and Saxena, R. (2012). Pharmacological Characterization and Beneficial Uses of Punica granatum. *Asian Journal of Plant Sciences*, **11**, 251-267.

Jones, M.M., Singh, P.K., Kostial, K., Blanus, M., Piasek, M. and Restek-Samarozija, N. (1997). Comparative in vivo lead mobilization of meso- and rac-2,3-dimercaptosuccinic acids in albino Wistar rats. *Pharmacol Toxicol*, **80**, 182–186.

Jurenka, J. (2008). Therapeutic applications of pomegranate (Punica granatumL.): a review. *Alternative Medicine Review*, **13**, 128-144.

Kalia, K. and Flora, S. (2005). Strategies for safe and effective therapeutic measures for chronic arsenic and lead poisoning. *Journal of Occupational Health*, **47**, 1-21.

Khan, M.S.H., Mostofa, M., Jahan, M.S., Sayed, M.A. and Hossain, M.A. (2008). Effect of garlic and vitamin B-complex in lead acetate induced toxicosis in mice. *Bangladesh Journal of Veterinary Medicine*, **6**, 203–210.

Kilikdar, D., Mukherjee, D., Mitra, E., Ghosh, A.K., Basu, A., Chandra M. and Bandyoapdhyay, D. (2011). Protective effect of aqueous garlic extract against lead-induced hepatic injury in rats. *Indian Journal of Experimental Biology*, **49**, 498-510.

Klaassen, C.D., Liu, J. and Choudhuri, S. (1999). Metallothionein: an intracellular protein to protect against cadmium tox-icity. Annual Review of *Pharmacology and Toxicology,* **39**, 267-294.

Kosnett, M. (2001). Lead. Clinical Toxicology. M. Ford, K. Delaney, L. Louis and T. Erickson. Philadelphia, Saunders.

DG, L.I., Zhang, Z.M. and Chen, X.J. (2003). Study on the influence of aqueous extract of leaves of punica granatum on the secretion of gastric acids and exprimental gastric ulcer. *Chinese Journal of Preventive Medicine*, **19**, 23-24.

Meldrum, J.B. and Kok, W. (2003). Effects of calcium disodium EDTA and meso-2, 3-dimercaptosuccinic acid of tissue concentrations of lead for use in treatment of calves with experimentally induced lead toxicosis. *American Journal of Veterinary Research,* **6**, 672–676.

Najar-Nezhad, V., Aslani, M.R. and Balali-

Mood, M. (2008). Evaluation of Allicin for the Treatment of Experimentally Induced Subacute Lead Poisoning in Sheep. *Biological Trace Element Research*, **126**, 141-147.

Needleman, H. (2009). Low level lead exposure: History and discovery. *Annals of Epidemiology*, **19**, 235-238.

Osman, M., Ahmed, M., Mahfouz, S. and Elaby, S. (2011). Biochemical Studies on The Hepatoprotective Effects of Pomegranate and Guava Ethanol Extracts. *New York Science Journal*, **4**, 27-39.

Patra, R.C. and Swarup, D. (2004). Effect of antioxidant ascorbic acid, l-methionine or α tocopherol alone or along with chelator on cardiac tissue of lead-treated rats. *Veterinarski arhiv*, **74**, 235-244.

Patrick, L. (2006a). Lead toxicity, a review of the literature. Part I: Exposure, evaluation, and treatment. *Alternative Medicine Review*, **11,** 2-22

Patrick, L. (2006b). Lead toxicity. Part II: The role of free radical damage and the use of antioxidants in the pathology and treatment of lead toxicity. Alternative *Medicine Review*, **11**, 114-126.

Petit, T.L., Alfano, D.P. and LeBoutillier, J.C. (1983). Early lead exposure and the hippocampus, a review and recent advances. *Neurotoxicology*, **4**, 79-94.

Shiban, M.S., Al-Otaibi, M. and Al-Zoreky, N.S. (2012). Antioxidant Activity of Pomegranate (Punica granatumL.) Fruit Peels. *Food and Nutrition Sciences*, **3**, 991-996.

Taubeneck, M.W., Domingo, J.L., Liobet, J.M. and Keen, C.L. (1992). Meso-2, 3-dimercaptosuccinic acid (DMSA) affects maternal and fetal copper metabolism in Swiss mice. *Toxicology*, **72**, 27-40.

Tendon, S.K., Singh, S. and Jain, V.K. (1994). Efficacy of combined chelation in lead intoxication. *Chemical Research in Toxicology*, **7**, 585–589.

Thuppil, V. and Kaushik, V.S. (2012). Future of Lead Chelation – Distribution and Treatment. *Journal of Krishna Institute of Medical Sciences University*, **1**, 6-23

Wang, R., Ding, Y., Rliu, R., Xiang, L. and Du, L. (2010). Pomegranate: Constituents, Bioactivities and Pharmacokinetics. *Fruit, Vegetable and Cereal Science and Biotechnology*, **4**, 77-87.

Zmudzki, J., Bratton, G.R. and Womac, C. (1983). Lead poisoning in cattle: reassessment of the minimum toxic oral dose. *Bulletin of Environment Contamination and Toxicology*, **30**, 435–441.

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بررسی اثرات درمانی عصاره پوسته سفید انار در مسمومیت با سرب در رت

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چکیده

انار یک میوه خوراکی با اثرات درمانی زیاد مثل اثرات آنتی اکسیدانتی، ضد التهابی و تنظیم کننده چربی خون است که از مدتها قبل شناخته شده است. در این مطالعه به بررسی اثرات درمانی عصاره پوسته سفید انار در درمان مسمومیت با سرب تجربی در رت پرداخته شده است. برای این منظور رتهای ماده، محلول ۱۰۰۰ppm استات سرب را بصورت آب خوراکی برای ۳۵ روز دریافت کردند. سپس حیوانات با عصاره پوسته سفید غشاهای داخلی انار (۱۰۰ mg/kg و ۲۰۰ mg/kg بصورت خوراکی) روزی دوبار برای ۳۵ روز درمان شدند. غلظت سرب در خون، کلیه، کبد، استخوان و مغز با دستگاه جذب اتمی اندازه گیری شد. عصاره پوسته سفید و غشاهای داخلی انار با دز بالاتر باعث کاهش غلظت سرب در مغز (۶۱٪)، خون (۵۳٪) و استخوان (۳۴.۵٪) شد. هیچ تغییر معنی داری در غلظت مس، روی و آهن سرم و کبد بدنبال تجویز عصاره پوسته سفید انار ایجاد نشد. در این مطالعه مشخص شد که عصاره پوسته سفید و غشاهای داخلی انار بدون هیچ تغییر معنی داری در المانهای ضروری خون و بافت، دارای اثرات درمانی بر مسمومیت با سرب در رت است.

واژگان کلیدی: انار، مسمومیت با سرب، میکرو المانها، رت